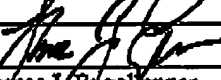
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Kimberly A. Gillis *et al.* Application No.: 09/996,630 - 3476 Filed: November 28, 2001 For: Expression Analysis of KIAA Nucleic Acid and Polypeptides Useful in the Diagnosis and Treatment of Prostate Cancer Attorney Docket No.: 102729-10	Group Art Unit: 1637 Examiner: Chunduru, Suryaprabha

Certificate of Mailing (37 C.F.R. 1.8(a))

I hereby certify that this correspondence is being deposited with the United States Postal Service Post Office as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date set forth below.

15 November 2004 Date of Signature and Mail Deposit		By:  Thomas J. Engellenner Reg. No: 28,711

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF STEVEN HANEY, PH.D.

PURSUANT TO 37 CFR §1.132

Dear Sir:

I, Steven Haney, a citizen of the United States residing at 72 Adams Road, Concord, MA 01742, hereby declare as follows:

1. I received a B.A. in biochemistry from the Stony Book University, NY in 1984 and was a awarded a Ph.D. in biochemistry from the University of Michigan in 1991. From 1991-1996, I was a Research Fellow at Princeton University, NJ. I am employed as a principal scientist in the Cancer Genetics Group at Wyeth located at 35 Cambridge Park Drive, Cambridge, MA 02140 and have been so employed since 2001. My responsibilities include conducting and supervising cancer genetic research, and in

particular, I am involved in profiling gene expression in human prostate tumors in comparison to cancer cell line models. Prior to taking this position in cancer genetics, I worked on genetic approaches to infectious diseases at Wyeth in Pearl River, NY for four years.

2. I am familiar with the above-identified patent application. I have reviewed the Office Action mailed July 15, 2004 with respect to the patent application at issue. I understand that this Office Action rejects the pending claims pursuant to 35 U.S.C. § 112, first paragraph, for not enabling one skilled in the art to make and/or use the invention.

3. I understand that the Examiner has asserted that the specification "does not provide any specific example that would easily predict a significant association of the level of expression of KIAA 18 or KIAA 96 with ... prostate cancer" and that the specification "fails to establish any correlation between the level of expression of KIAA markers and the prostate cancer" since the specification relies on *in vitro* data.

4. Based on my knowledge and experience in the field, and I believe and declare that one skilled in the art would recognize that the LNCaP cell line model used in the experiments described in the application is a well-characterized model of human prostate cancer. Consequently, an increase in KIAA 18 expression and a decrease in KIAA 96 expression in the LNCaP cell line model is indeed predictive that expression of these markers would likewise vary in cancer tissue.

5. Well-characterized human cancer cell lines, such as LNCaP, are routinely used and have proven to be highly predictive of *in vivo* results. The LNCaP cell line, which was established from a metastatic lesion of human prostatic adenocarcinoma, has been widely used in the study of prostate cancer for over 20 years. The enclosed seminal journal article establishes the LNCaP cell line maintains malignant properties, hormonal responsiveness and drug

sensitivity of the prostate adenocarcinoma (Horoszewicz, J.S. "LNCaP Model of Human Prostatic Carcinoma" *Cancer Research*, 43, 1809-1818 (1983)). Those skilled in the art view LNCaP cells as an established *in vitro* model of prostate cancer as evidenced by the fact that this seminal article establishing the LNCaP cell line has been cited over 800 times in other peer-reviewed journals.

6. Recent articles have verified that the LNCaP model of human prostate cancer progression and metastasis "closely mimics the genetic and pathological processes of cancer growth and progression in men" (Thalmann, G.N., et al. "LNCaP Progression Model of Human Prostate Cancer: Androgen-Independence and Osseous Metastasis" *The Prostate* 44: 91-103 (2000)). The LNCaP cell model expresses prostatic acid phosphatase, androgen receptor, and PSA, which is a hallmark of the prostatic phenotype and an invaluable marker of prostate cancer progression.

7. As described in the specification of the application at issue, the identified markers, KIAA 18 and KIAA 96, were found to be significantly ($p<0.05$) and differentially expressed between the diseased and normal tissues. The LNCaP well-established cell line model of human prostate cancer was used to show that KIAA 18 increase and KIAA 96 decrease in expression in prostate cancer cells after androgen treatment. The prostate specific antigen (PSA) gene, which is recognized in the art as a diagnostic marker of prostate cancer, was used as an internal control showing that change in expression of KIAA 18 and KIAA 96 corresponds to the expected increase in PSA expression in prostate cancer cells. In addition, analysis of RNA from human solid prostate tumors with different Gleason scores compared to normal prostate tissue verified that the differential expression of KIAA 18 and KIAA 96 corresponds with increase in tumor grade.

8. Therefore, one skilled in the art would appreciate the accuracy with which the cell line model of prostate cancer mimics the genetics of human prostate cancer and further recognize the application's analytical techniques (e.g., RNA extraction, quantitative RT-PCR, western blot analysis, statistical analysis, and tissue microarray analysis) to be well established. One skilled in the art would conclude, as I have, that the *in vitro* data presented by the applicant is well correlated with the invention as claimed, namely the methods of the invention to diagnose or monitor development or progression of prostate cancer in humans.

9. I further declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: October 14th, 2005

Steven Haney, Ph.D.
Principal Scientist II
Wyeth

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